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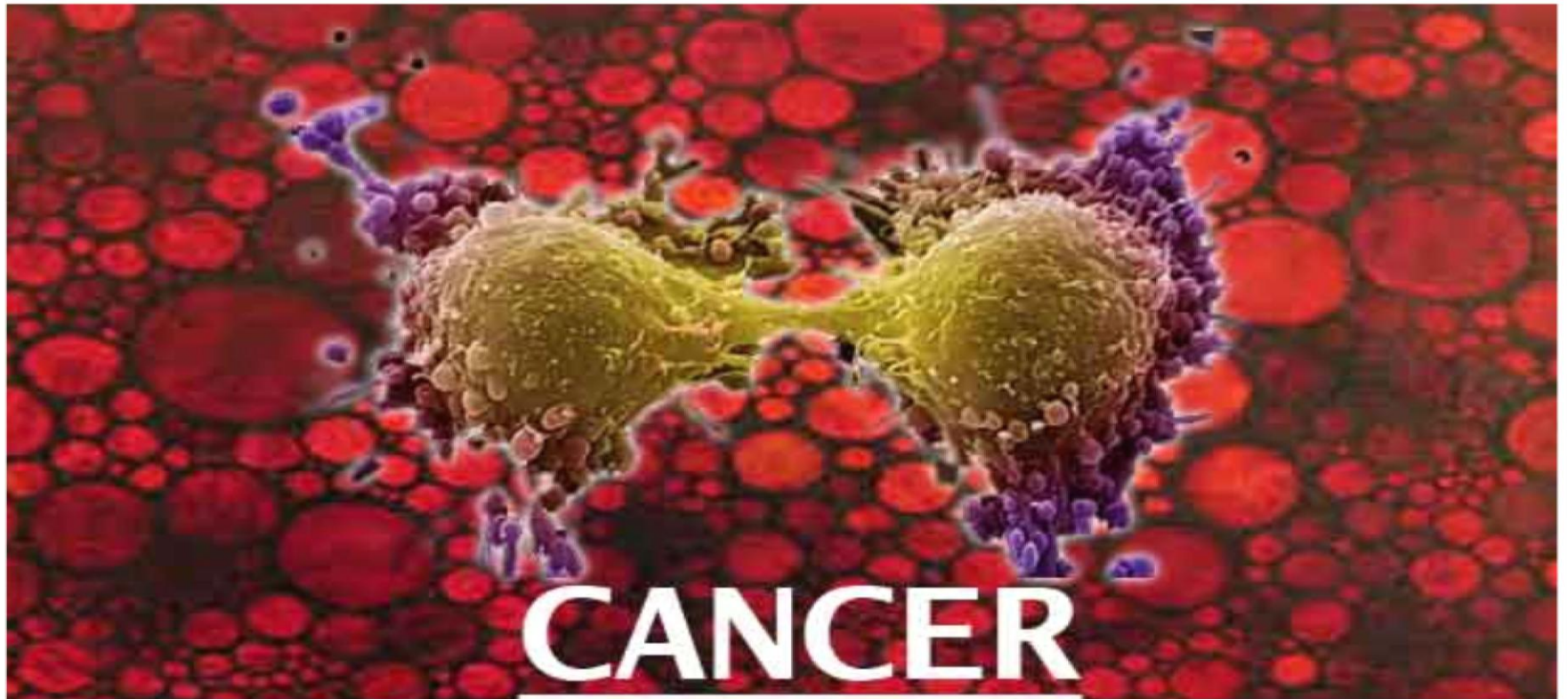
Effects of unsaturated fatty acids on cancer

Overview



- Cancer
- Unsaturated fatty acids
- PUFAs and signaling pathways in cancer
- PUFAs and cancer

Cancer:

Disease of cells .It is caused by the disruption of the orderly process of cell growth.(Rebecca S. et al, Cancer Statistics, 2013)



Cancer has two aspects:

- ✓ Environment (about 90 %)
- ✓ Genetics (about 10%)
 - Environmental causes such as smoking, diet and obesity, radiation, infection, stress, lack of physical activity and environmental pollution
 - Genetic factors can be classified into two groups:
 1. Oncogenes  lead to cell growth
 2. Tumor suppressor  an important role in controlling cell growth and division.

❑ The most important **oncogenes** such as:


ERK ,MYC,WNT,RAS and TRK

❑ The most important **Tumor suppressor** such as:

p15,p16,p18,p19,p21,p27 and p53

Other factors has a role in cancer development :

✓ **Epigenetic changes** including **hypermethylation** and **Hypomethylation** in the DNA level.

■ Hypermethylation promoter region of suppressor gene 
reduction in the translation of this genes and uncontrolled growth of cells.

➤ Irregularities in the cell cycle  A very important factor in the pathology of cancer.

Genomic changes in cancer



causing mutation



Production oncogenic genes with dominant performance



The loss of the tumor suppressor gene function



abnormal and excessive cell growth

Cancer statistics

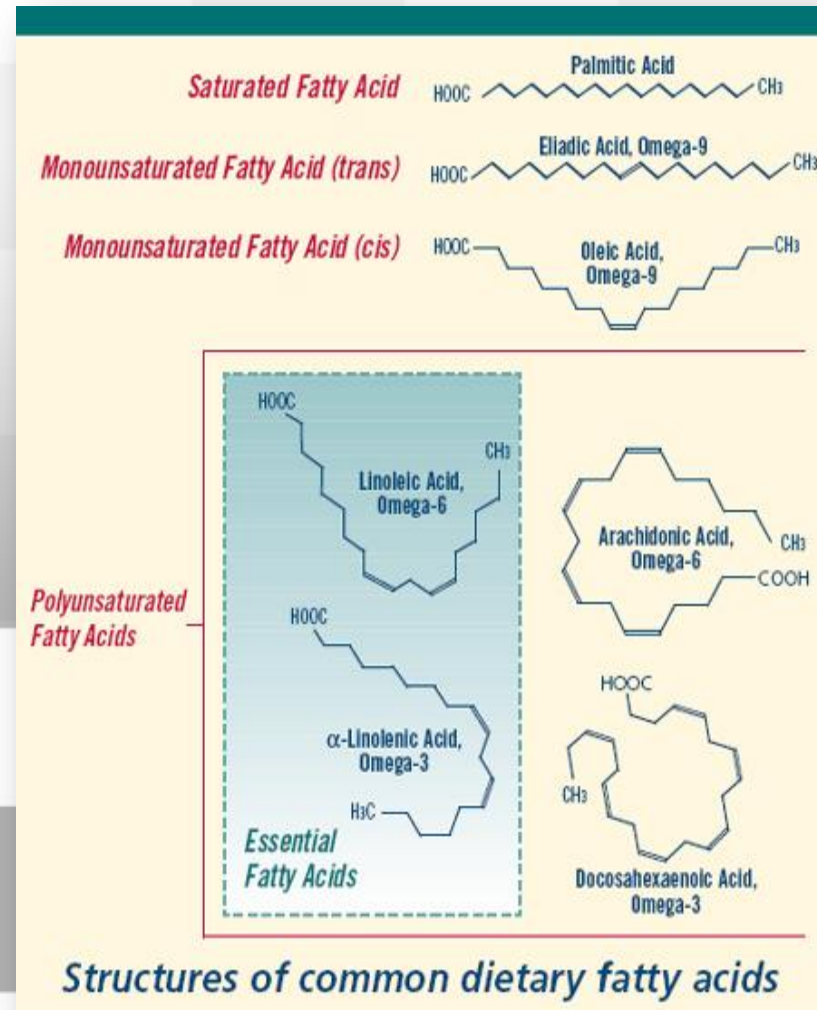
- **Cancer is the third main cause of death in Iran**
- **The 5 most common cancers in males:**
 - **stomach (26.1 per 105), esophagus (17.6), colon-rectum (8.3), bladder (8.0) and leukemia (4.8)**
- **The 5 most common cancers in females:**
 - **breast (17.1), esophagus (14.4), stomach (11.1), colon-rectum (6.5) and cervix uteri (4.5).**
- **The incidence rates of esophageal and stomach cancer in Iran are high.**



Unsaturated fatty acids

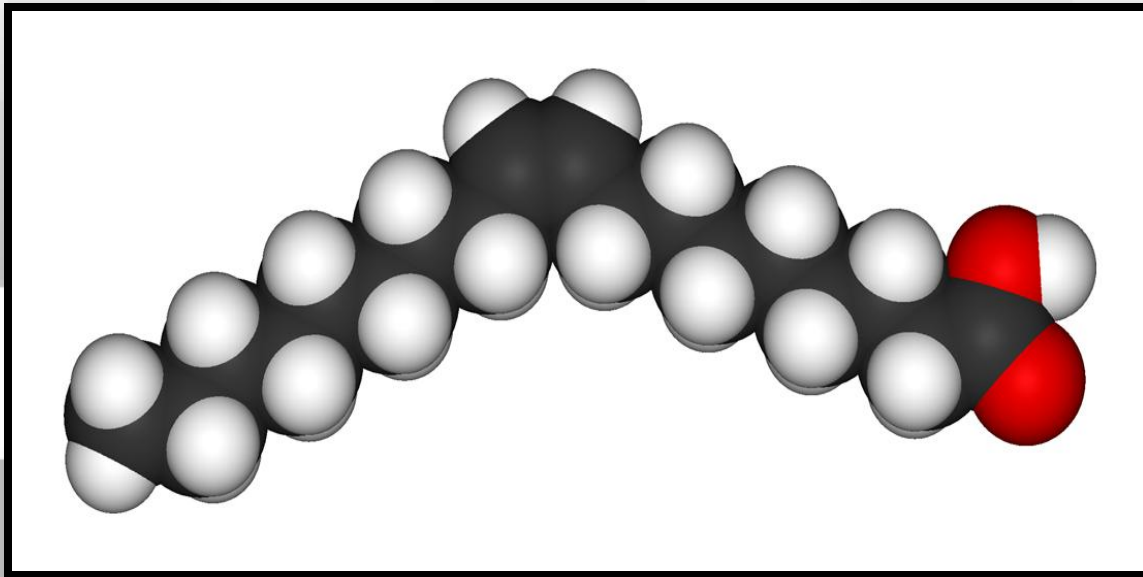
➤ **MUFAs** : Monounsaturated fatty acids

➤ **PUFAs** : Polyunsaturated fatty acids:



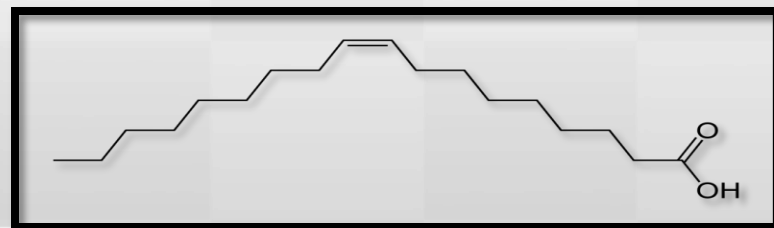
MUFAs

MUFAs (MonoUnsaturated Fatty Acids) are fatty acids that have **one double bond** in the fatty acid chain and all of the remainder of the carbon atoms in the chain are single-bonded.

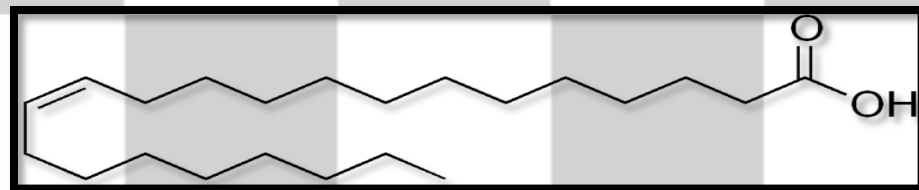


Omega-9 fatty acids

- **Omega-9 fatty acids (ω -9 fatty acids or n -9 fatty acids) :**
a family of unsaturated fatty acids which have in common a final carbon-carbon double bond in the omega-9 position.
- Two important omega-9 fatty acids are:
 - **Oleic acid (18:1, n -9)**, which is a main component of **olive oil**

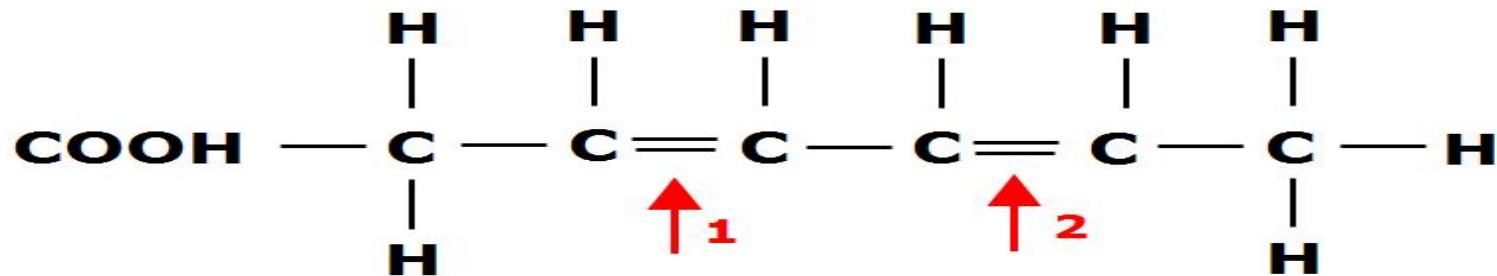


- **Erucic acid (22:1, n -9)**, which is found in **mustard seed**



PUFAs

- **Polyunsaturated fatty acids (PUFAs)** are fatty acids that contain **more than one double bond** in their backbone. This class includes many important compounds, such as **essential fatty acid**.

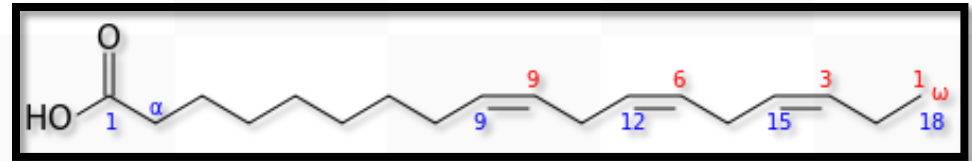


Polyunsaturated Fat

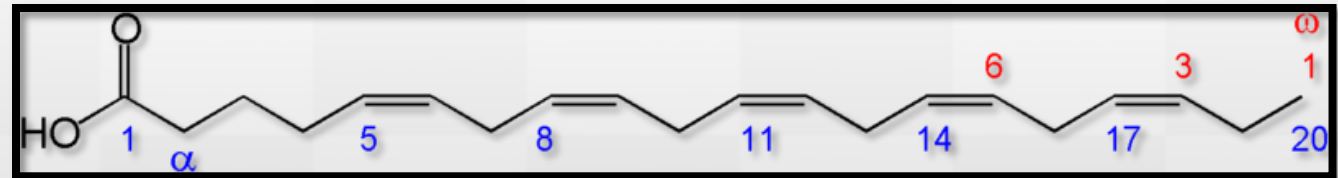
Omega-3 fatty acid

- ❖ Omega-3 fatty acids (also called ω -3 fatty acids or *n*-3 fatty acids) are polyunsaturated fatty acids with a double bond (C=C) at the **third carbon atom from the end of the carbon chain**.
- ❖ The fatty acids have two ends, the **acid (-COOH) end**, which is considered the beginning of the chain, thus "**alpha**", and the **methyl (CH₃) end**, which is considered the "**tail**" of the chain, thus "**omega**." The nomenclature of the fatty acid is taken from the **location of the first double bond**, counted from the **methyl end**, that is, the **omega (ω -) or the n- end**.

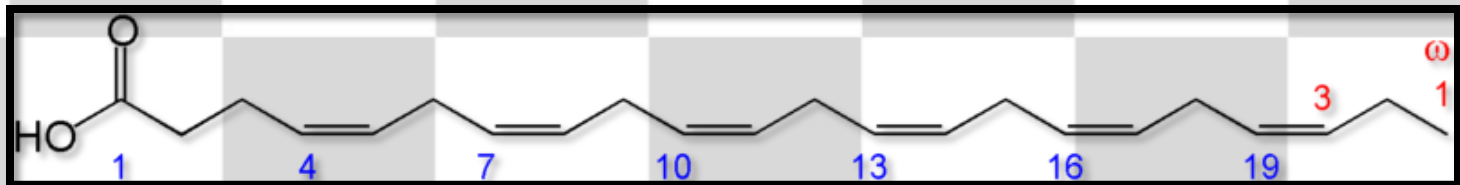
- **ALA or α -Linolenic acid** (found in plant oils)
(18:3n-3)



- **EPA or Eicosapentaenoic acid**
(20:5n-3)



- **DHA or Docosahexaenoic acid** (both commonly found in marine oils).
(22:6n-3)



Omega-6 fatty acid

- ❖ Subscribers called omega-6 polyunsaturated fatty acids with long chain (LCPUFAs)
- ❖ an unsaturated carbon in the sixth position of the methyl end
- ❖ Components of essential fatty acids
- ❖ Phospholipids vital component of cell membranes and a precursor of the large number of metabolites

The first member of w6:

❑ Linoleic acid (LA), a fatty acid of 18 carbons with two double bonds (18: 2)

❑ Features LA:

✓ lack synthesized by humans and get it from food

✓ Changes after taking it includes:

▪ More saturated and prolonging it

▪ Converting it into other form such as Gamma-Linolenic acid (GLA)(18:3 ω -6)

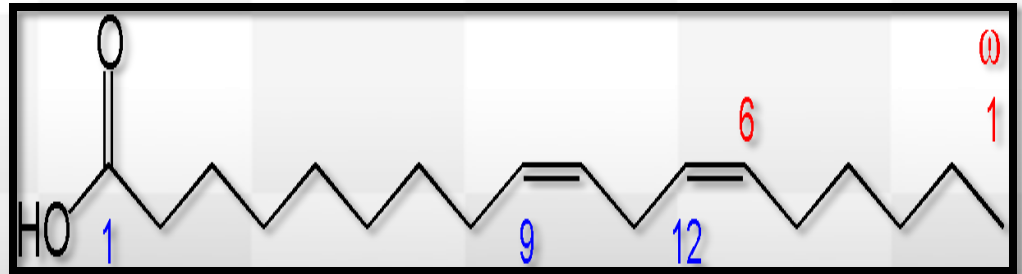
▪ The next state is converted to arachidonic acid(AA)(20:4 ω -6), an important omega-6 in metabolism

➤ AA be found in meat, eggs and some fish .

Omega-6 fatty acids refer to a group of two fats called :

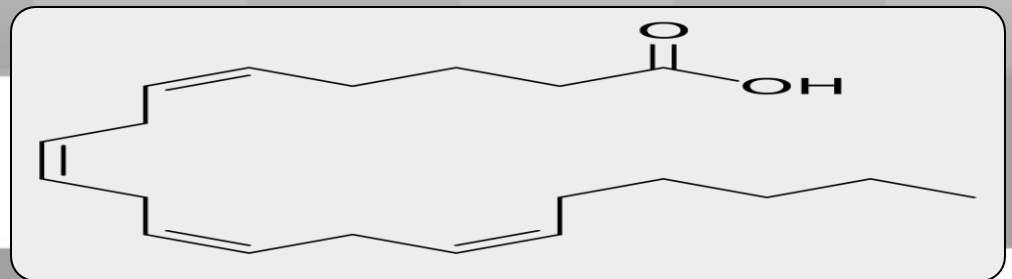
➤ Linoleic acid (LA)

■ Formula: $C_{18}H_{32}O_2$



➤ Arachidonic acid

■ Formula: $C_{20}H_{32}O_2$



TYPES OF FATTY ACIDS

(according to the number of double bonds)



Saturated (No bond)



Monounsaturated (1 bond)



Polyunsaturated (>1 bond)



PUFAs and signaling pathways in cancer

Wnt signaling pathway

❖ The term Wnt is a combination of the Drosophila gene *wingless* and the homologous mouse proto-oncogene *Int-1*.

❖ One of the most important cell signaling pathways

Signal transmission through this route to 3 as follows:


1. Wnt/ β -catenin pathway: the canonical pathway
2. Wnt/ Ca^{2+} pathway: a non-canonical pathway
3. PCP(planar cell polarity) pathway: a non-canonical pathway

The canonical pathway :

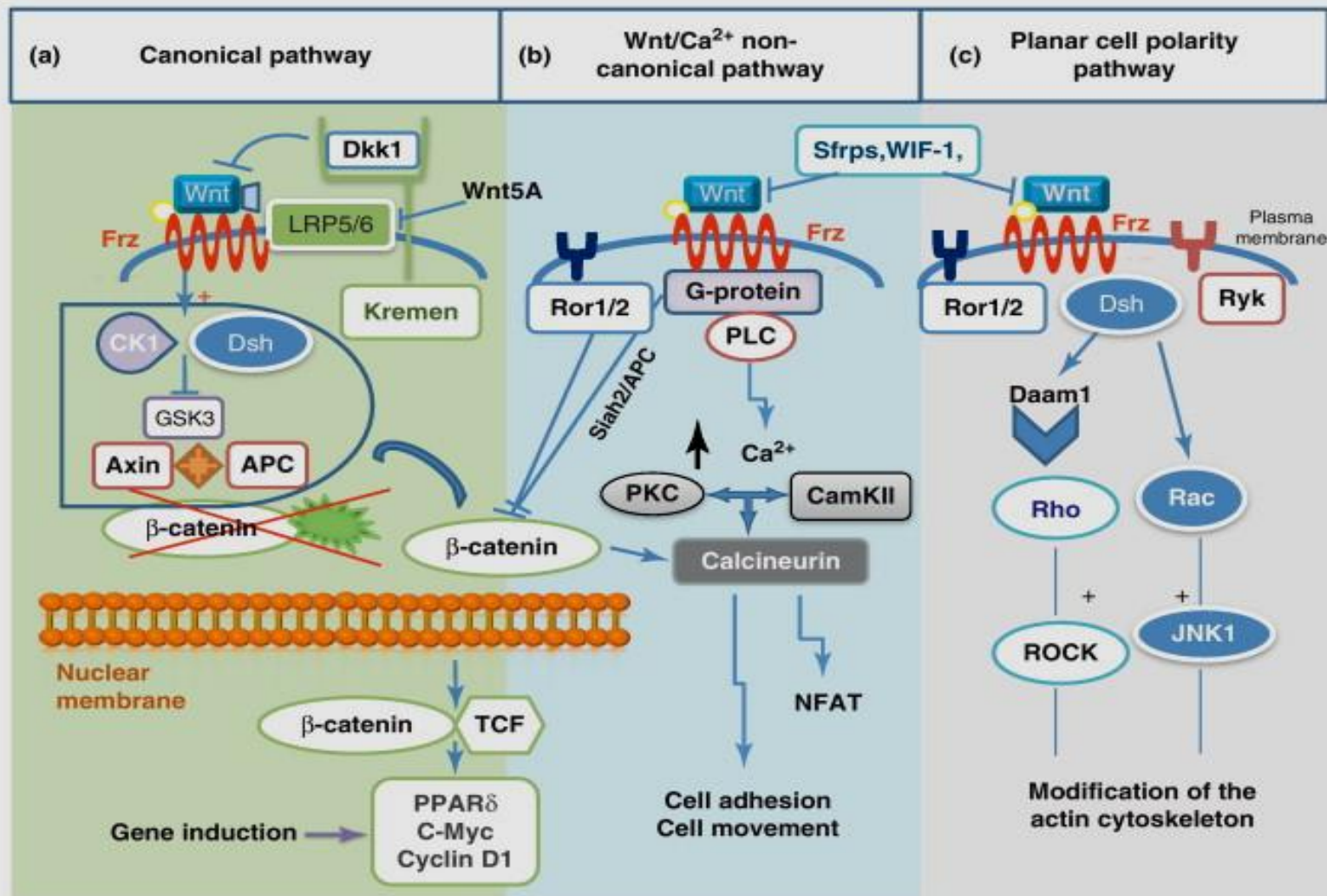
development, tissue homeostasis, and Mitotic divisions and cancer

❑ Therefore Failure to set the pathway leads to abnormal proliferation and chromosomal instability, which is a sign of cancer

1. Wnt/ β -catenin pathway: the canonical pathway

- involves the transcriptional coactivator β -catenin.
- In the absence of Wnts  β -catenin is degraded by a multiprotein complex consisting of axin, glycogen synthase kinase 3b (GSK-3b), and the adenomatosis polyposis coli (APC).

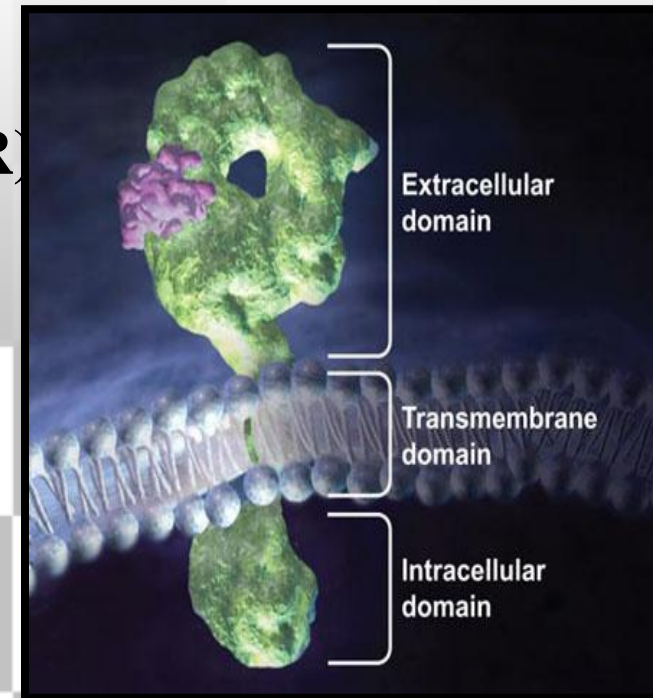
A schematic representation of the Wnt signaling pathway



TRENDS in Endocrinology & Metabolism

Receptor Tyrosine Kinases

- Protein tyrosine kinases (PTKs) play an important role in the **signal transduction pathways** that control **cell proliferation** and **differentiation**, and are involved in **tumorigenesis**.
- Almost all human cancers display **dysregulated expression**
- PTKs such as :
 - **epidermal growth factor receptor (EGFR)**
 - **tropomyosin receptor kinase B (trk B)**represent potential targets for **cancer**.



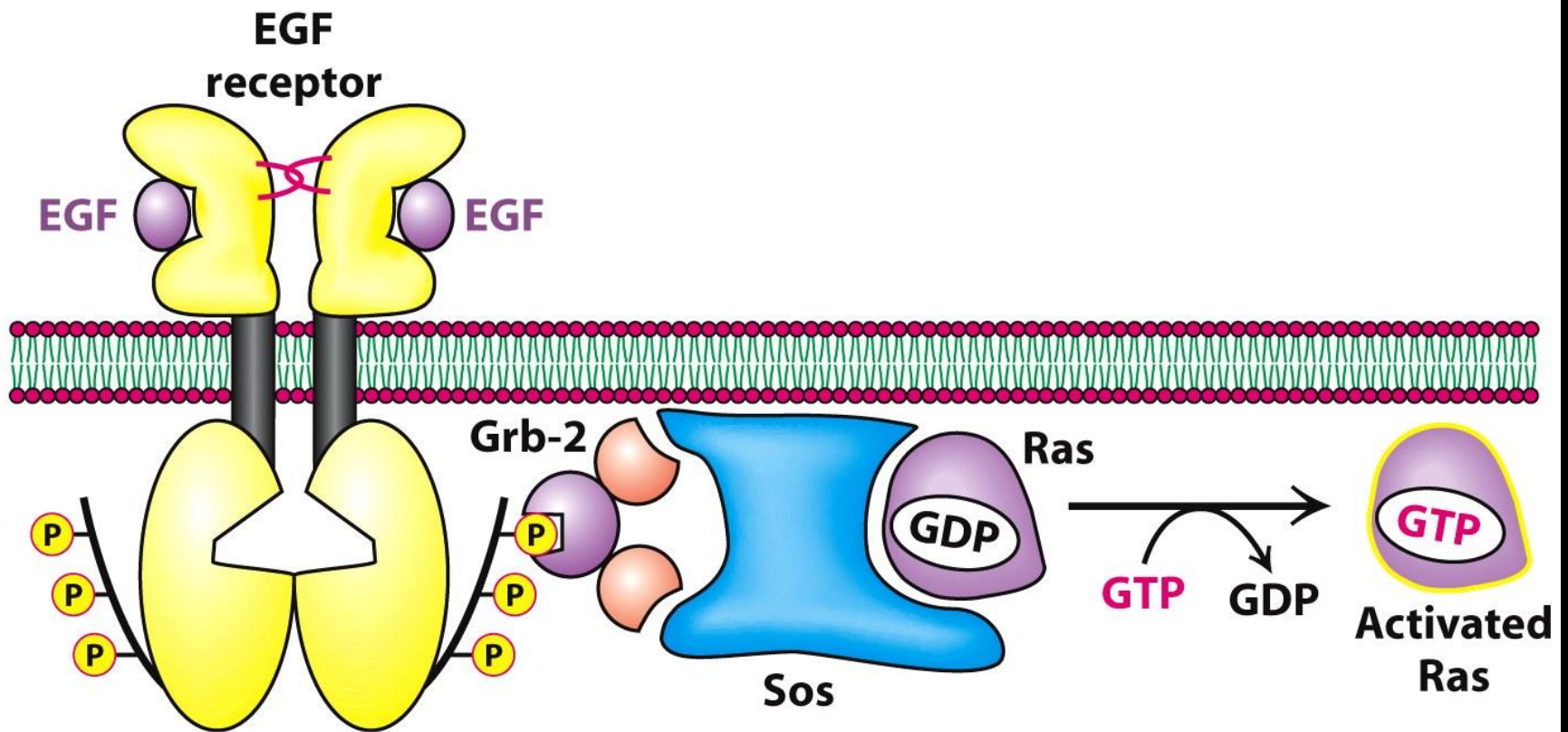
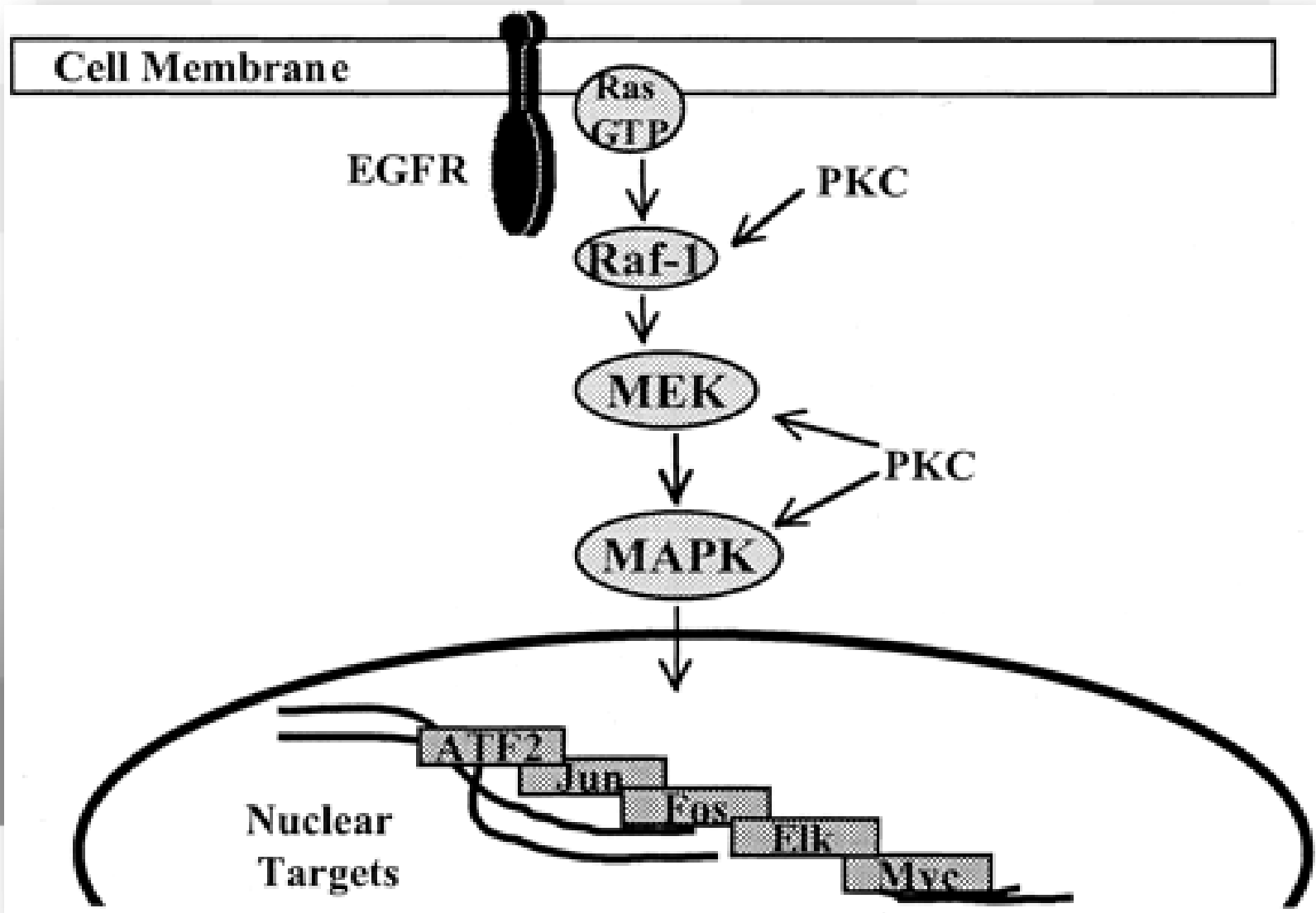


Figure 14.30

Biochemistry, Seventh Edition

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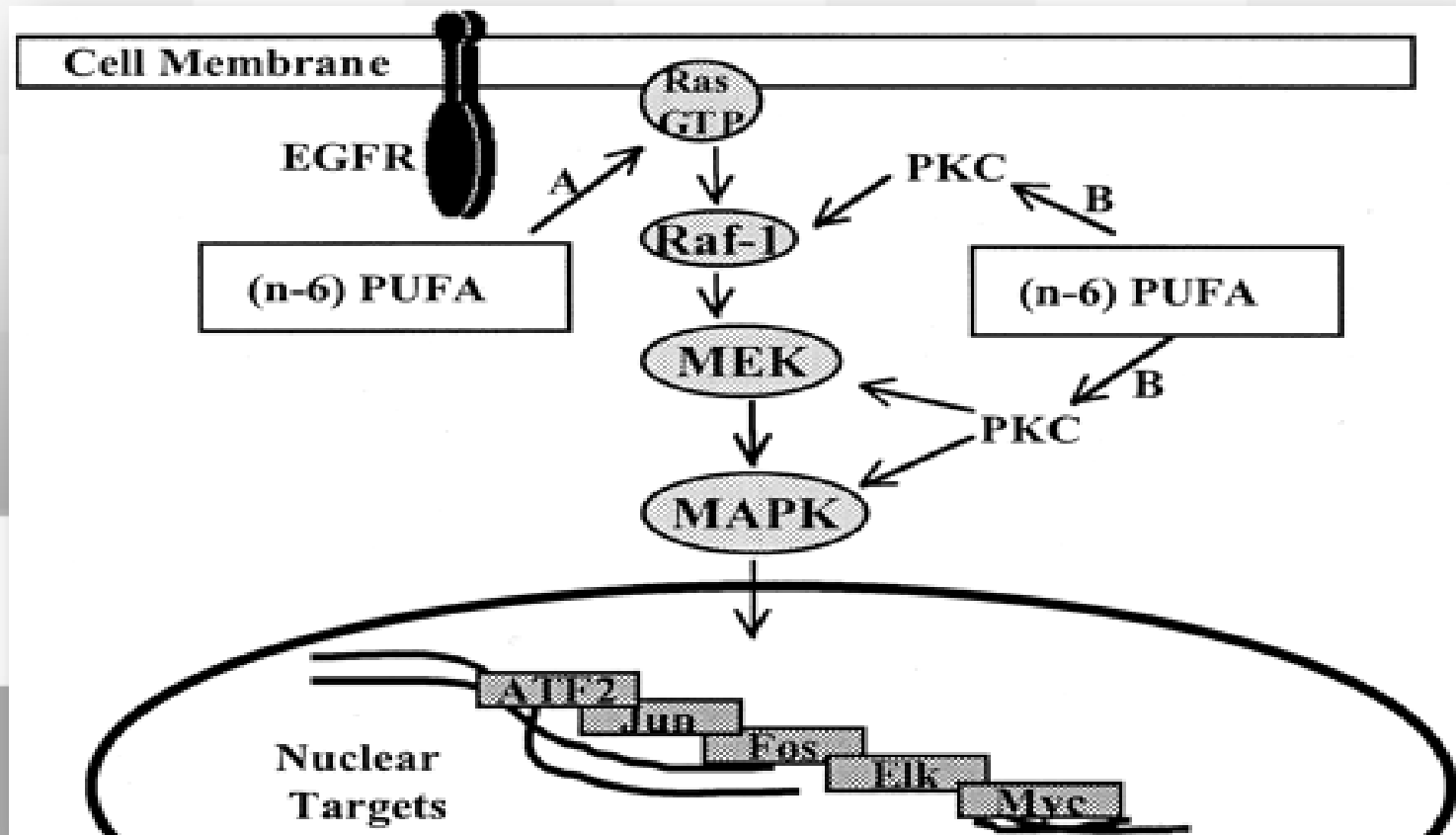
Trk B and cancer

- Tropomyosin receptor kinase B (Trk B) is part of the large family of **receptor tyrosine kinases** affecting **neuronal survival** and **differentiation** through several signal cascades.
- Trks **regulate important processes** in **non neuronal cells** and, in addition to their impact on **tumors of neural origin**, may contribute to the pathogenesis of **ovarian** and **prostate** tumors.

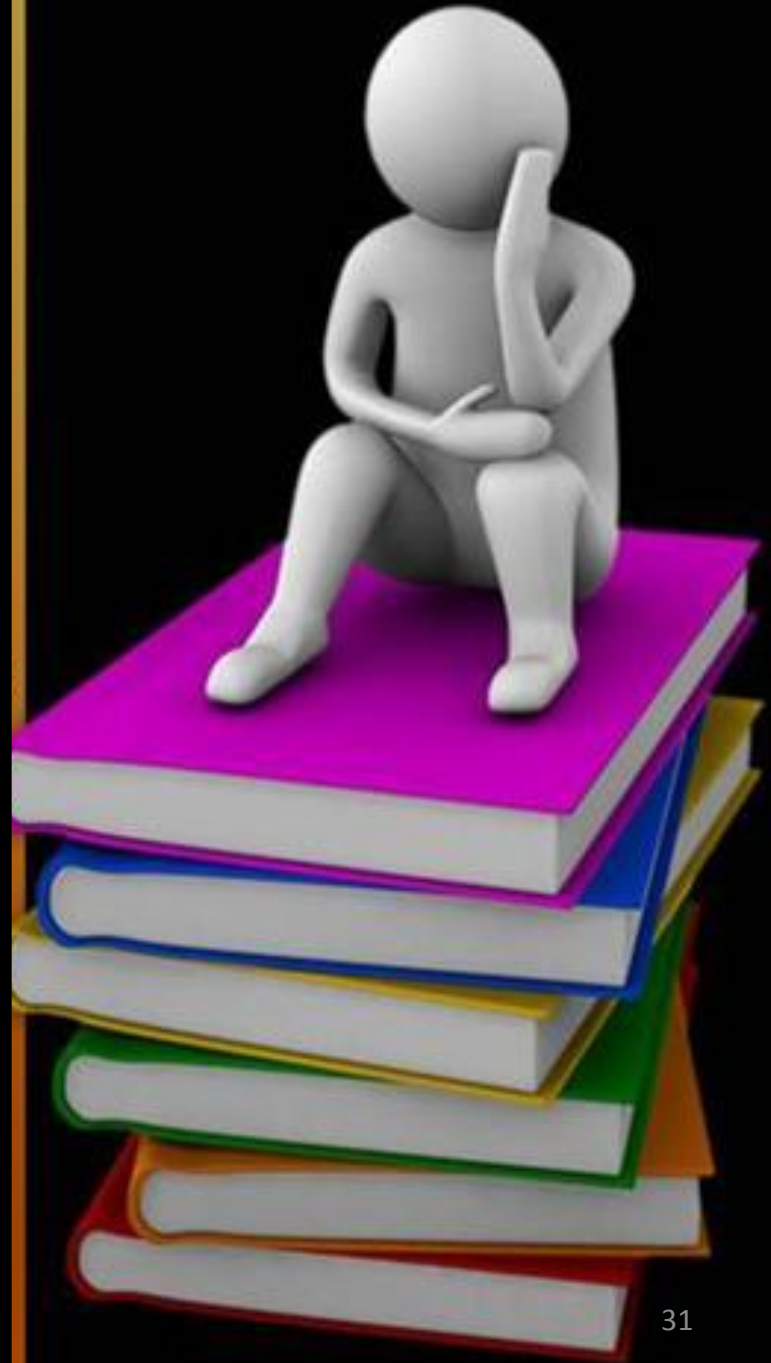
PUFA and EGFR/Mitogen-Activated Protein Kinase

- ❑ The involvement of **MAPK** in the **progression of mammary cancer** is supported by much research.
- ❑ A major role of **MAPK** is to modulate **enzymes** and **gene transcription** involved in **cellular proliferation**.
- ❑ Studies show that dietary **PUFA** may **regulate** the **growth** and **progression of mammary cancer** through the **modulation of EGFR**.
- ❑ Researchers have demonstrated that **AA** can **inhibit GTPase-activating proteins (GAPs)**, which are involved in the hydrolysis of **GTP-bound (active) Ras protein** in the **EGFR/MAPK cascade**.

- ❖ (n-6) PUFA have been implicated in the **activation** of several isoforms of **protein kinase C (PKC)**, which are **effectors** of **MAPK signaling**.



PUFAs and cancer



- both **epidemiological** and **animal** studies have reported a **protective role** of **oleic acid (n-9 MUFA)** in **several cancers** such as **breast, colorectal** and **prostate** cancers.
- The **n-3 PUFAs** might alter the **growth of tumour cells** by
 - ✓ **influencing cell replication**, by interfering with **components of the cell cycle**
 - ✓ **increasing cell death** either by way of **necrosis** or **apoptosis**.

Studies have shown that Arachidonic acid (**AA**), Eicosapentaenoic acid (**EPA**) and Docosahexaenoic acid (**DHA**) are caused apoptosis and reduced proliferation of cancer cells. Oxidative stress may play different roles in the pathogenesis of skin cancer in humans. Compare the effects of AA, EPA and DHA on the survival of melanoma cells was shown that all these PUFs have inhibitory effects on cell proliferation of melanoma. The results were statistically significant and returning to levels PUFs . According to the results ,anti-proliferative effects of fatty acids in human melanoma cells depends to acid type, concentration and melanoma cell lines.

✓ Epidemiological studies on the relationship between PUFAs with cancers of the total offer:

➤ **The protective effects of n-3PUFAs** against cancer

➤ **The stimulating effects of n-6PUFAs (dose dependent)** against cancer.

✓ high-fat diet has an impact on the development of **prostate cancer**. Unsaturated fats have bad effects on tumor formation. In the family of polyunsaturated fats, **ω-6 increases the risk and ω-3 reduces it.**

Thank
you



